

November 4, 1959

Dr. H. R. Holman
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Dear Hal:

I was interested to read your editorial on SLE in the October 1959, "American Journal of Medicine." I would like to ask you just one question in connection with your view of this disease: Is there any substance for which you do not find some antibodies in the sera of SLE patients? It would be amusing, for example, to titrate a few sera against a number of rare Salmonella h. antigens. From some of your remarks I guess that you would predict that you would get reactions with a wide variety of antigens. If this is the case, then the apparent auto-immunity is only a small facet of the total generalized response. In viewing this disease then, I think it would be a mistake to adhere too closely to the usual concept of antibodies being produced as a "reaction" to the corresponding antigen. I am, of course, thinking back to our theory of spontaneous antibody formation subject to subsequent selection.

You commented elsewhere on the genetic relationships between SLE and agammaglobulinemia. What may be common to the two diseases is the incapacity to make a specific response to a particular antigen. But whereas in agammaglobulinemia there is no response at all, in SLE you get this generalized response. I would hesitate to guess what the genetic or physiological connections must be to convert one disease into the other. It might be worth looking carefully at whether normal lymphoid cells give an SLE-like response in agammaglobulinemic individuals (which raises some cautions for the conduct of such clinical experiments) or the converse, whether spleen or marrow implants from agammaglobulinemia into, say irradiated animals, give an SLE-like serum effect. These are both very long shots, of course,

We are trying hard to set up the sera that you sent us. Unfortunately, we are having some difficulties with the florescent side of the technique but hope to have these ironed out before long.

Yours sincerely,

Joshua Lederberg
Professor of Genetics

P.S. Would you be kind enough to send a reprint or two of that article? I believe I have already asked you to keep us on your list for general distribution.